DETAILED ACTION

Claims 1-29 are pending in this application.

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-29) in the reply filed on 07/27/08 is acknowledged. Applicant's election with traverse of the species (effector molecules-growth factors), (cellular components-bacteria), (detector molecules-specific dyes), (cellular responses-growth inhibition) and (molecule of interest-small organic molecules) in the reply filed on 07/27/08 is acknowledged. The traversal is on the ground(s) that it would not place an undue burden on the examiner to search both bacteria and mammalian cells concurrently. This is found persuasive and the species "mammalian cells" is rejoined.

The requirement is still deemed proper and is therefore made FINAL.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office (EPO 03447276.1) on 11/28/2003. It is noted, however, that applicant has not filed a certified copy of the EPO application as required by 35 U.S.C. 119(b).

Drawings

The drawings are objected to because Figure 3 refers to a view from the side with reference letter "b". However the Figure contains reference letter "S" in its place. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s).

See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 6-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 and 31 of U.S. Patent No. 7,419,778 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the methods teach essentially the same method utilizing the same aluminum oxide porous substrate and method steps for the purposes of assaying the responses of cells or viruses on the surface of the substrate to effector molecules or test compounds. For example, the instant application teaches a method for screening of cellular responses of viruses, cells or components thereof comprising:

(a) providing a solid porous support having first and second surfaces and at least one area with a plurality of through-going channels;

(b) providing viruses, cells or components thereof on said first and/or second surface of said solid porous support, wherein said solid porous support retains said viruses, ceils or components thereof on its surface, wherein said viruses, cells or components thereof are viruses, mammalian cells, insect cells, yeast cells, fungal cells, plant cells, bacteria, cellular vesicles, cellular organelles, tissue sections, whole organisms or nematodes, or components thereof;

(c) providing a supply chamber at said first and/or second surface and opposite to said cellular components;

(d) subjecting all or part of said viruses, cells or components thereof to one or more effector molecules; wherein at least one effector molecule is delivered from said supply chamber through the porous support, wherein said effector molecules are nutrients, enzyme substrates, test compounds, inducer molecules, chaperone proteins, hormones, oligopeptides, nucleic acids, agonists, antagonists, inhibitors of cellular functions, enhancers of cellular functions, transcription factors, growth factors, differentiation-inducing agents, secondary metabolites, toxins, glycolipids, carbohydrates, antibiotics, mutagens, drugs, proteins, antibodies, antibody fragments, modified analogues thereof, or any combination thereof;

(e) incubating the said all or part of said viruses, cells or components thereof with said effector molecules under conditions allowing the induction of cellular responses in the said all or part of said viruses, cells or components thereof, wherein said responses are chemically-induced or physiological events in said cells or viruses; lysis, apoptosis, growth inhibition, growth promotion, morphology changes, cell differentiation, organelle movement, changes in metabolite concentrations or metabolite patterns; changes in cellular contents; changes in mRNA level, protein composition, lipid composition or carbohydrate composition; production, secretion or surface exposure of a protein or a molecule of interest by said cells; membrane surface molecule activation, receptor activation or trans-membrane ion transports; stage of infection to viruses, prions or cellular pathogens or resistance to such pathogens; or cell-cell interactions, or changes to communities or mixtures of cells;

(f) optionally providing detector molecules to the said all or part of said viruses, cells or components thereof for assaying said responses, wherein said detector molecules are nucleic acids, peptides, proteins, antibodies, antibody fragments, aptamers, enzyme substrates, carbohydrates, or specific dyes and wherein said detector molecules are appropriate to detect responses to be assayed;

(g) assaying for responses using detector molecules, wherein said detector molecules are nucleic acids, peptides, proteins, antibodies, antibody fragments, aptamers, enzyme substrates, carbohydrates, or specific dyes; and

(h) identifying and characterizing the responses induced by said effector molecules

Conflicting Patent '778 teaches a method for screening of cellular responses of viruses, cells or cellular components thereof comprising:

(a) providing cells or cellular components on the surface of a solid porous metallo-oxide substrate, wherein said cells or cellular components are mammalian cells, insect cells, yeast cells, fungal cells, plant cells, bacteria, viruses or components thereof, and wherein

(i) said solid porous substrate has oriented through-going channels;

(ii) said solid porous substrate retains said cells or cellular components on the substrate surface, and wherein,

(iii) said solid porous substrate has immobilized therein, within the pores, an array of detector molecules, wherein said detector molecules are nucleic acids, peptides, proteins, antibodies, antibody fragments, enzyme substrates or specific dyes and wherein said detector molecules are appropriate to detect cellular responses to be assayed;

(b) delivering test compounds to positions on the substrate corresponding to the arrayed detector molecules on the surface of said solid porous substrate;

(c) incubating said test compounds with said viruses, cells or cellular components on the surface of the solid porous substrate, under conditions allowing the induction of cellular responses, wherein said cellular responses are chemically-induced or physiological events in said cells; production, secretion or surface exposure of a molecule of interest by said cells; membrane surface molecule activation; receptor activation; transmembrane ion transports; or transcriptional regulations;

(d) assaying said cellular responses, wherein cellular responses are detected using said detector molecules; and, identifying and characterizing the cellular responses induced by said test compounds.

As can be seen by comparison the differences between the two methods are minor in nature and would have been obvious to one of ordinary skill in the art at the time of the invention. For example the instant application requires the presence of a supply chamber at said first and/or second surface and opposite to said viruses, cells or components thereof, wherein the supply chamber comprises at least one compartment and is provided with a liquid medium comprising at least one effector molecule.

Further, the instant application has an optional step wherein detector molecules are provided to the viruses, cells or components thereof for purposes of assaying the cellular responses induced by the effector molecules. While the '778 Patent does not specify by what means the test compounds are delivered to the viruses, cells or components thereof, it would have been obvious to one of ordinary skill in the art that a pipette containing the test compound (a test compound can be an effector molecule) would meet all of the limitations pertaining to a supply chamber in instant application claims 1-3. Further, the '778 patent requires that the detector molecules be arrayed in the pores of the solid, porous flow through substrate. However, those of ordinary skill in the art would have recognized that the instant application does not indicate the location of the detector molecules and therefore one of ordinary skill in the art would have found obvious their placement in the pores of the substrate as there are limited numbers of positions that the detector molecules can be arrayed in. All other limitations are met with some specificity in the claims cited above pertaining to the conflicting US Patent but for purposes of brevity have not been cited.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7, 9, 11, 12, 14, 15, 18, 21, 23 and 24-27 are rejected under 35 U.S.C. § 102(b) as being anticipated by Soole *et al.* (1992).

Soole *et al.* teaches a method comprising providing a solid polycarbonate or aluminum metal-oxide membrane tissue culture inserts (inherently having first and second surfaces and through-going channels or pores), seeding either transfected canine kidney (MDCK) or transfected human colonic adenocarcinoma (Caco-2) cells directly onto the surface of the inserts wherein the MDCK and Caco-2 cells are retained, placing the inserts into 6-well plates containing either 0.5 or 1mg/ml of the drug G418 sulphate respectively wherein the inserts are in liquid contact with the medium containing wells and incubating the cells for 3-5 days for MDCK and 7-28 days for Caco-2 cells and determining the time to reach confluency (Pg. 496, Column 2, Lines 44-51) and determining the secretion of the enzyme endoglucanase E' Methylumbelliferyl cellobiosidase (MUCase) lysing samples of the cells and determining a change in fluorescence (Pg. 497, Column 1, Lines 43-59), wherein the morphology of transfected cells was observed via electron microscopy and wherein it was determined that transfected cells reached confluency 24 hours later than non-transfected cells, indicative of growth inhibition (Pg. 497, Column 2, Lines 40-45 and 54 and Pg. 498, Column 1, Lines 1-3).

It is inherent in the method of Soole *et al.* that the media containing the effector molecules is transported passively or diffuses through the porous solid support because the pores of the support are small enough to retain the cells on the surface but still are sufficient to let medium containing nutrients pass though to reach the cells residing on the cell culture inserts, barring any evidence to the contrary.

Claims 1-3, 7-9, 11-13, 16, 18, 21 and 23-27 are rejected under 35 U.S.C. § 102(b) as being anticipated by Churchouse *et al.* (US 4,963,490).

Churchouse *et al.* teaches a method comprising providing an aluminum oxide porous solid support having a first and second surfaces and a plurality of through-going channels or pores, applying a culture of mammalian cells to a surface of the solid support wherein the solid support retains the cells on its surface, providing a supply chamber at the second surface and opposite the cells (a well), incubating the cells in growth medium (containing nutrients or the drugs dexamethasone or insulin, or "effector molecules") which perfuse passively by contact force through the porous solid support from the supply chamber and determining the cell growth (concentration and viability) by delivering Erythrocin B dye to the cell medium resuspended cells and identifying the number of viable cells at various timepoints and wherein cells grown on porous solid membranes can be readily observed using light microscopy (Column 9, Lines 10-33, Columns 11 and 12, Claims 1, 3, 4, 5, 6 and 7 and Figure 2).

Claims 1-9, 11-16, 18, 19, 21-23 and 26-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Leoni *et al.* (2002).

Leoni *et al.* teaches a method comprising providing a porous solid support having a first and second surfaces and a plurality of through-going channels or pores, applying a culture of mammalian cells to a surface of the solid support wherein the solid support retains the cells on its surface, providing a supply chamber at the second surface and opposite the cells (a well), incubating the cells in growth medium (containing glucose or albumin, growth factors (Fetal Bovine Serum) or "effector molecules") which perfuse passively by contact force through the porous solid support from the supply chamber and determining the cell growth (concentration and viability) by delivering the intracellular fluorescent dye carboxyfluorescein diacetate succinimidyl ester (CFDA) to the cell medium resuspended and pelleted cells and identifying the number of viable cells and degree of proliferation at various timepoints by measuring fluorescence and wherein cells grown on porous solid membranes can be readily observed using light microscopy and wherein the cells can be pre-labeled with CFDA prior to culturing; and wherein the diffusion of glucose and albumin percentage rates per hour based on membrane pore size are determined, which inherently constitutes a gradient of the two effector molecules in two dimensions (time and space) (Pg. 119, Lines 3-28 and Pg. 11, Figures 3 and 4, Pg. 115, Figure 7).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 7, 9, 11, 12, 14, 15, 18, 20, 21, 23 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soole *et al.* (1992).

The teachings of Soole *et al.* were discussed above.

Soole *et al.* did not teach a method wherein delivery of the effector molecules is from above the support by manual means.

It would have been obvious to one of ordinary skill in the art to apply culture medium from above into the porous cell inserts containing the cells because those of ordinary skill in the art would have recognized that culture medium is routinely pipetted by hand onto cell cultures in microbiology laboratories.

Claims 1-3, 7-9, 11-13, 16,18, 20, 21 and 23-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Churchouse *et al.* (US 4,963,490).

The teachings of Churchouse *et al.* were discussed above.

Churchouse *et al.* does not teach a method wherein delivery of the effector molecules is from above the support by manual means.

It would have been obvious to one of ordinary skill in the art to apply culture medium from above into the porous membrane supports containing the cells because those of ordinary skill in the art would have recognized that culture medium is routinely pipetted by hand onto cell cultures in microbiology laboratories.

Claims 1-23 and 26-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Leoni *et al.* (2002).

The teachings of Leoni *et al.* were discussed above.

Leoni *et al.* does not teach wherein the effector molecule(s) is/are transported actively through the porous solid support by pumping, magnetically, electrically or by piezo-electronic force, wherein the effector molecule is a drug selected from a chemical or natural drug candidate library, or wherein delivery of the effector molecules is from above the support by manual means. It would have been obvious to one of ordinary skill in the art to apply culture medium from above into the porous membrane supports containing the cells because those of ordinary skill in the art would have recognized that culture medium is routinely pipetted by hand onto cell cultures in microbiology laboratories. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to actively transport the effector molecules through the solid support rather than relying on passive diffusion in order to decrease the time required to perform the experiments. One of ordinary skill in the art would have been motivated to make this change in order to more effectively use time-sensitive test agents, such as isotopes with short half-lives or light or oxygen sensitive compounds.

One of ordinary skill in the art would have recognized that the choice of an effector compound which is selected from a drug or natural chemical library is an obvious source of potential test compounds. Those of ordinary skill in the art would have been aware of catalogs or web sites containing a myriad of drugs and/or chemicals available for screening assays. For example, the Sigma-Aldritch company catalog lists many thousands of drugs and chemicals.

Claim 29 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No Claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ingham *et al.* "The micro-petri dish, a million-well growth chip for the culture and high-throughput screening of microorganisms"; PNAS, Vol. 104, No. 46 (2007) pp. 18217-18222.

Ingham *et al.* "Growth and Multiplexed Analysis of Microorganisms on a Subdivided, Highly Porous, Inorganic Chip Manufactured from Anopore"; Applied and Environmental Microbiology, Vol. 71, No. 12 (2005) pp. 8978-8981.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL C. MARTIN whose telephone number is (571)272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

10/20/08

/JON P WEBER/

Supervisory Patent Examiner, Art Unit 1657